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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/684,774	10/14/2003	Richard S. Dondero	CELL-0276	3355
23377	7590	06/01/2006	EXAMINER GUDIBANDE, SATYANARAYAN R	
WOODCOCK WASHBURN LLP ONE LIBERTY PLACE, 46TH FLOOR 1650 MARKET STREET PHILADELPHIA, PA 19103			ART UNIT	PAPER NUMBER 1654

DATE MAILED: 06/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/684,774	DONDERO ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Satyanarayana R. Gudibande	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 15 May 2006.  
 2a) This action is FINAL.                    2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-6 and 8-20 is/are pending in the application.  
 4a) Of the above claim(s) 1-6 is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 8-20 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | Paper No(s)/Mail Date. _____ .  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>11/21/03</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
|   | 6) <input type="checkbox"/> Other: _____ .                                  |

## **DETAILED ACTION**

### *Election/Restrictions*

Applicant's election with traverse of group II invention in the reply filed on 5/15/06 is acknowledged. The traversal is on the ground(s) that separate and diverse searches would not be required for the present application. This is not found persuasive because the product as claimed could be used in a materially different process and hence search for the product would not result in the process for which it is intended. Therefore, the two groups of inventions belong to separate status in the art as shown by their different classification.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-6 have been withdrawn from further consideration as being drawn to non-elected invention.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 8-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 91/01143 of Pillai, et al., in view of US 5,286,847 issued to Gehrke, et al and further in view of Beissert, et al., The Journal of Investigative Dermatology, 1998, 111, 609-615.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

In the instant application, applicants claim a method of modulating immune response of a subject to a vaccine antigen comprising administering an effective amount of IL-1 mutein having reduced toxicity, in concurrent or sequential combination with said vaccine antigen.

Pillai, et al., teaches a method of eliciting an immune response against an antigen comprising administering to a vertebrate host an effective amount of a composition comprising a mixture of an antigen and an interleukin along with a pharmaceutically acceptable carrier (claims 34-37 on page 27). The reference teaches administration of several antigens (as listed in claim 37) via variety of ways such as intramuscular, intra-peritoneal, intravenous, subcutaneous, oral and intranasal routes (lines 27-30 on page 6; and lines 1-2 on page 7). The reference does not explicitly teach the use of IL-1 mutein but teaches the use of other interleukin species.

Gehrke, et al., teaches use of IL-1 muteins that encompasses the replacement of the positively charged Arg amino acid of IL-1 $\beta$  with Gly at position 127 that results in reduced biological activity but retain their receptor binding affinity and immunogenic activity (column 4, lines 23-31). The reference further teaches that the positively charged amino acids could be replaced with any of the other 17 natural amino acids and the one of the specific position at

which there is no change in the binding affinity but dramatic change in the biological activity is Arg127 in human IL-1  $\beta$  precursor (column 2, lines 1-14).

Beissert teaches the difference between the use of IL-1 $\alpha$  and IL-1 $\beta$  in eliciting immune response to tumor-associated antigen when treated the Langerhans cell-enriched preparations of epidermal cells with a combination of antigen and the IL-1 $\alpha$  or IL-1 $\beta$  (abstract). The results indicated IL-1 $\beta$  enhanced the number of specific antibody producing spleen cells where as IL-1 $\alpha$  was inhibitory (page 614, column 1, paragraph 2).

It would have been obvious to one of ordinary skill in the art to modify the method of eliciting an immune response by administering a stable vaccine composition comprising a mixture of interleukin and the antigen taught by Pillai in light of the teachings of Gehrke and Beissert, et al. Although, Pillai does not teach the use of IL-1 mutein, it teaches the administration of a combination of interleukin and the antigen, one would be motivated to modify the method to use the IL-1 $\beta$  mutant which has high receptor binding affinity but significantly reduced activity. There would have been reasonable expectation of success given the knowledge that IL-1 $\beta$  is enhanced the number of specific antibody producing spleen cells where as IL-1 $\alpha$  was inhibitory when a combination of the interleukin and antigen was administered to Langerhans cell-enriched preparations of epidermal cells as taught by Beissert, et al. Therefore, the invention as a whole was clearly a *prima facie* obvious to one skilled in the art at the time the invention was made.

### ***Conclusion***

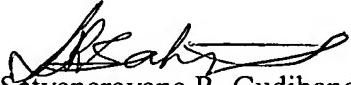
No claim is allowed.

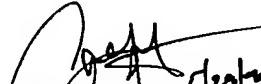
Art Unit: 1654

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Satyanarayana R. Gudibande whose telephone number is 571-272-8146. The examiner can normally be reached on M-F 8-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Satyanarayana R. Gudibande, Ph.D.  
Art Unit 1654

  
ANISH GUPTA  
PRIMARY EXAMINER